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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/730,790	12/05/2000	Mark H. Tuszynski	041673/2047	8867

30542 7590 10/20/2004

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EXAMINER

CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/730,790

**Applicant(s)**

TUSZYNSKI ET AL.

**Examiner**

Shin-Lin Chen

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 6,9 and 10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,5,7,8 and 11-20 is/are rejected.
- 7) ☒ Claim(s) 3 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

Applicants' amendment filed 6-24-04 has been entered. Claims 1, 5 and 14 have been amended. Claims 16-20 have been added. Claims 1-20 are pending. Claims 1-5, 7, 8 and 11-20 are under consideration.

#### ***Terminal Disclaimer***

1. The terminal disclaimer filed on 6-24-04 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent No. 6,683,058 has been reviewed and is accepted. The terminal disclaimer has been recorded.

#### ***Priority***

The present application claims priority of Application No. 09/060,543, filed 4-15-98, however, Application No. 09/060,543 fails to disclose a method for ameliorating neuronal atrophy and loss accompanying normal aging in the mammalian brain by delivering a transgene encoding a growth factor to preselected sites in the brain. Therefore, the claimed priority for the subject matter of "a method for ameliorating neuronal atrophy and loss accompanying normal aging in the mammalian brain by delivering a transgene encoding a growth factor to preselected sites in the brain" is not granted.

#### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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3. Claims 5, 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants' amendment filed 6-24-04 necessitates this new ground of rejection.

The phrase "the neurotrophin encoding transgene composition is delivered directly" on lines 1-2 of claim 5 is vague and renders the claim indefinite. It is unclear to what location said composition is delivered to. Claims 7 and 8 depend on claim 5 but fail to clarify the indefiniteness.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 4, 5, 7, 8 and 11-15 remain rejected and newly added claims 16-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for ameliorating neuronal loss accompanying normal aging in the mammalian brain by directly delivering an expression vector, such as a viral vector, comprising a transgene encoding NGF to preselected delivery sites in the brain, and the targeted cholinergic neurons are within 500 um of a delivery site, and the disclosure by Mandel et al., 1999 and Felgner et al., 1996, as discussed below, does not reasonably provide enablement for a method for ameliorating neuronal atrophy and loss accompanying normal aging in a mammalian brain by directly or indirectly administering a neurotrophin encoding transgene in any vector to a preselected delivery site in

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the brain via various administration routes *in vivo*, wherein the targeted neurons are located more than 500  $\mu\text{m}$  from a delivery site or the delivery site is remote from the targeted neurons. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 2-19-04. Applicant's arguments filed 6-24-04 have been fully considered but they are not persuasive.

Applicants argue that the route of administration of the present invention is amended to be "directly", which corresponds to the *in vivo* means claimed in US Patent 6,683,058 ('058), and "indirectly", which corresponds to the *ex vivo* means claimed in US Patent 6,451,306 ('306). Applicants further argue that since the claims in '058 and '306 are enabled, therefore, the claimed invention of the present application is enabled (amendment, p. 11-12). This it not found persuasive because of the reasons set forth in the preceding Official action mailed 2-19-04. The claimed invention of '306 requires use of genetically modified donor cells to ameliorate the defective, damaged or diseased brain cells. As discussed in the preceding Official action mailed 2-19-04, grafting cells secreting NGF into a mammalian brain is different from administering transgene into a mammalian brain. The claims of the present invention read on gene therapy *in vivo* and the state of the art for gene therapy was unpredictable at the time of the invention. The biggest problems hampering successful gene therapy is the ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time. The fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, and

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the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced are all important factors for a successful gene therapy. Administration route also plays an important role in determining gene transfer efficiency in vivo. Further, '306 has limitation that each grafting site is no more than about 500 um from a defective, diseased or damaged brain cell and no more than about 5 mm from any other grafting site. Patent '508 has limitation that the transgene is directly delivered to the brain and is expressed in, or within 500 um from, a targeted cell, and no more than about 10 mm from another delivery site. However, the claimed invention does not have those limitations. Thus, the enablement of the claimed inventions of '306 and '508 do not conflict with the enablement rejection under 35 U.S.C. 112 first paragraph for the claimed invention of the present application.

### ***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 5 and 7 remain rejected under 35 U.S.C. 102(b) as being anticipated by Kojima et al., 1997 (Biochemical and Biophysical Research Communications, Vol. 238, p. 569-573, IDS-A1) claims and is repeated for the reasons set forth in the preceding Official action mailed

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2-19-04. Applicant's arguments filed 6-24-04 have been fully considered but they are not persuasive.

Applicants fail to provide any argument for this 35 U.S.C. 102(b) rejection in the amendment filed 6-24-04. Therefore, the claims remain rejected for the reasons set forth in the preceding official action mailed 2-19-04.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 5, 7 and 8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mandel et al., 1999 (Experimental Neurology, Vol. 155, No. 1, pp. 59-64) and is repeated for the reasons set forth in the preceding Official action mailed 2-19-04. Applicant's arguments filed 6-24-04 have been fully considered but they are not persuasive.

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Applicants fail to provide any argument for this 35 U.S.C. 103(a) rejection in the amendment filed 6-24-04. Therefore, the claims remain rejected for the reasons set forth in the preceding official action mailed 2-19-04.

***Conclusion***

11. Claims 1, 2, 4, 5, 7, 8 and 11-20 are rejected. Claim 3 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.



**SHIN-LIN CHEN  
PRIMARY EXAMINER**